REMARKS

Claims 1-16 are pending in this application.

The Amendments are intended to clarify the scope and priority of the invention, and to expedite processing of allowable claims. Certain claims are re-written for convenience and expediency, and not as a reflection on the contemplated scope or propriety of those or any other claims. These amendments are not intended or considered to narrow any of the claims in any manner, including without limitation for any statutory, patentability, or other reason.

Duplicate Claim Warning

Claims 11, 15, 16; 4, 5, 12; and 13, respectively, are noted to be objectionable under 37 C.F.R. § 1.75 over claims 1; 3; and 6, should claims 1, 3, and 6 be found allowable, as being a substantial duplicate thereof.

Claims 11, 12, and 13 are cancelled above. Claims 15 and 16 are amended to depend from claim 1, rather than from now-cancelled claim 11.

Applicants respectfully suggest that claims 4 and 5, and amended claims 15 and 16, are not substantial duplicates of claims 1, 3, or 6, because each of claims 4, 5, 15, and 16 adds a distinct limitation regarding formulation of the composition particularly for administration to a unique and specific body cavity -- the subject's vaginal cavity, buccal cavity, nasal cavity, or rectal cavity, respectively. None of these specific sites of administration is referred to in any other claim in the application. Thus, the various claims include various combinations of significant limitations.

Applicants respectfully suggest that such limitations distinguish claims 4, 5, 15, and 16 from the other pending claims. Formulations designed for a particular body cavity may have, for

example, different properties, or different adjuvants or additives, than formulations designed for other body cavities, or for general use. For example, the anticipated mode of administration, such as by a sprayer, tube, suppository, or tablet, often dictates certain properties of a composition to be administered, such as form, thickness, etc. Clearly it also may be preferable for a composition intended for administration to a specific body cavity to have a special degree or quality of consistency, texture, smoothness, feel, fragrance, liquidity, viscosity, degree of bioadhesion, pH, or various other relevant properties. As a specific example, a formulation for nasal administration typically would have very different characteristics than a formulation for rectal administration, which would usually be very different from a formulation for oral administration. Accordingly, claims 4, 5, 15, and 16 should be considered to be sufficiently distinct from the other pending claims.

Rejection of Claims Under 35 U.S.C. § 102

Claims 1, 3-5, 7-9, 11-13, 15, 16 are rejected as being anticipated by Bologna U.S. Patent No. 5,543,150 ("Bologna" or "the '150 patent"). Bologna is said to disclose "a composition comprising progesterone, cross-linked polycarboxylic acid (polycarbophil), and water soluble polymer (Carbopol 934P)." Bologna is said to teach "a method of delivering the composition to a mucosal surface (vaginal cavity)."

As amended, the pending claims all address progressive hydration compositions and use of progressive hydration compositions. In contrast, Bologna discloses formulations for vaginal administration, which not designed to provide, and indeed are not capable of providing, progressive hydration.

By their very nature, the Bologna vaginal formulations disclosed already are mixed with water, such as in a gel or suspension, in order to provide the desired bioadhesion and convenience. *See, e.g.,* col. 6, lines 1-3 (noting that the composition can be squeezed through a plunger, applied in a douche, or applied manually). *See also, e.g.*, col. 5, lines 51-57 and 63-64; col. 6, lines 51-52. Every dose administered in the Example in Bologna involved an aqueous formulation. See col. 6, lines 44-60.

Further, Bologna discloses and discusses only bioadhesive, aqueous formulations. There is absolutely no disclosure or discussion in Bologna of any progressive hydration formulation. Nor does Bologna disclose or suggest in any manner a need of, or use for, progressive hydration formulations.

In stark contrast, the instant invention contemplates formulations that progressively hydrate, protecting the inner core from moisture and the surrounding environment for an extended period of time. *See, e.g.*, specification, at page. 7, lines 13-16. The water soluble polymer provides bioadhesion sooner, as soon a the outside starts to wet, while the water-insoluble polymer provides bioadhesion later, as it swells. Thus, the instant formulation uses only formulations intended at least in part to stay dry for an extended time, while Bologna discloses only 'wet' formulations that already include water and/or that are intended immediately to absorb water, swell, and adhere. The mere presence of several of the same ingredients in a composition that is prepared very differently does not result in a product with similar properties.

Thus, Bologna, which should be deemed mutually exclusive with the instant invention, does not disclose or discuss the instant progressive hydration invention.

Rejection of Claims Under 35 U.S.C. § 103(a)

Claim 2 is rejected as being unpatentable over Bologna as applied above to claims 1, 3-5, 7-9, 11-13, 15, 16, in further view of Bologna. Bologna is said to teach all that is recited in claim 2 "except for the composition/method comprising progesterone in about 50% or less." The office action notes that one of ordinary skill in the art "would have expected to determine the optimum amount of progesterone through routine experimentation. One would have been motivated to do this in order to make a composition and to develop a process that would supply progesterone to the vagina."

As discussed above, Bologna does not discuss or disclose any progressive hydration formulation. Instead, Bologna is mutually exclusive with the instant invention, using only wet formulations compared to the instant dry formulations. Thus, the instant claims, including claim 2, are not obvious over or anticipated by Bologna. Because claim 1 is not unpatentable over Bologna for obviousness or anticipation, claim 2, which depends from claim 1 and adds an additional limitation, cannot be obvious over Bologna.

Rejection of Claims for Obviousness-Type Double Patenting

Claims 1-5, 7-9, 11-13, 15, and 16 are rejected under the judicially created doctrine of obviousness-type double patenting, over claims 1-3, 6-8, 10, 13-16 of Bologna (U.S. Patent No. 5,543,150). An appropriate terminal disclaimer was requested. The Examiner also noted that, at the time, U.S. application no. 09/379,310 was unavailable to the Examiner. The Examiner requested that we provide in this application a copy of the allowed claims in 09/379,310.

First, U.S. application no. 09/379,310 is the parent application to this application. A copy of the allowed claims in that case as transcribed by Applicants is attached hereto.

Second, as discussed above, Bologna is mutually exclusive with the instant invention. Bologna discloses aqueous vaginal preparations for administration of progesterone. In contrast, the instant invention discloses dry, progressive hydration formulations for extended, protected release of treating agents including agents sensitive to pH or moisture. Nothing in Bologna makes obvious a preparation specifically intended to allow progressive hydration and release of such sensitive treating agents. Applicants respectfully request that this rejection be withdrawn.

Claim Objection/Allowable Subject Matter

Claims 6, 10, 14 are objected to as being dependent on rejected base claims, but they are said to be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 6, 10, and 14 have been re-written in independent form, including all of the limitations of the base and intervening claims. Applicants respectfully suggest that these claims, at the very least, are now in condition for allowance.

Conclusion

In light of the above remarks, Applicants respectfully request reconsideration and withdrawal of the rejections and objection, and respectfully solicit a Notice of Allowance. If it would be

convenient to the Examiner, Applicants' patent attorney may be reached at the Washington, D.C. telephone number provided below.

Respectfully submitted,

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Dated: April 24, 2001 By: _____

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CLAIMS ALLOWED
U.S. Pat. App. No. 09/379,310; our ref. 251/157 US (23)

Claims 1-5 and 7-26

1. A sustained release, progressive hydration bioadhesive tablet comprising:

an effective amount of active ingredient selected from the group consisting of glycoproteins, proteins, sex hormones, anti-hormones, nitrates, beta-agonists, beta-antagonists, opioids, opioid-antagonists, antidepressants, HMG CoA reductase inhibitors, antihistamines, ACE inhibitors, prostaglandins, and any other active ingredient which is metabolized or degraded by moisture, enzymes or pH,

about 5% to about 50% by weight cellulose,

about .5% to about 25% by weight starch,

about 1% to about 50% by weight lactose,

about .5% to about 10% by weight water insoluble cross-linked polycarboxylic polymer, and

about 1% to about 75% by weight water soluble polymer.

2. The tablet of claim 1, wherein said tablet comprises between a minuscule amount and about 50% by weight active ingredient.

3. The table of claim 2, further comprising:

about 1% by weight silica.

4. The tablet of claim 3, further comprising:

about .5% to about 2% by weight talc.

5. The tablet of claim 4, further comprising:

about .5% to about 1% by weight magnesium stearate.

7. The tablet of claim 5, wherein said starch is present in about 2% to about 10% by weight, said lactose is present in about 8% to 16% by weight, and said water soluble polymer is present in about 25% to about 35% by weight, and

wherein said tablet is adapted for delivering said active ingredient to the bloodstream of a patient via the patient's vaginal cavity.

8. The tablet of claim 5, wherein said starch is present in about 14% to 24% by weight,

said lactose is present in about 17% to 27% by weight, sand said water soluble polymer is present in about 5% to about 20% by weight, and

wherein said tablet is adapted for delivering said active ingredient to the bloodstream of a patient via the patient's buccal cavity.

9. A sustained release, progressive hydration bioadhesive tablet comprising:

an effective amount of an active ingredient selected from the group consisting of glycoproteins, proteins, sex hormones, anti-hormones, nitrates, beta-agonists, beta-antagonists, opioids, opioid-antagonists, antidepressants, HMG CoA reductase inhibitors, antihistamines, ACE inhibitors, prostaglandins, and any other active ingredient which is metabolized or degraded by moisture, enzymes or pH,

about 2% to about 30% by weight binder,

about 5% to about 40% by weight lactose,

about 1% to about 3% by weight water insoluble cross-linked polycarboxylic polymer, and

about 5% to about 50% by weight water soluble polymer.

10. The tablet of claim 9, further comprising:

about .2 to 2% by weight silica.

11. The tablet of claim 10, further comprising:

about .5% to about 2% by weight talc.

12. The tablet of claim 11, further comprising:

about .5% to about 2% by weight magnesium stearate.

13. The tablet of claim 12 wherein said active ingredient is testosterone and said testosterone is present in an amount of about 1% to about 30% by weight.

14. The tablet of claim 13, wherein said binder is starch and is present in about 2% to about 10% by weight, said lactose is present in about 8% to 16% by weight, said water soluble polymer is present in about 25% to about 35% by weight, and

said tablet is adapted for delivering said active ingredient to the bloodstream of a patient via the patient's vaginal cavity.

15. The tablet of claim 13, wherein said starch is present in about 14% to 24% by weight,

said lactose is present in about 17% to 27% by weight, said water soluble polymer is present in about 5% to about 20% by weight, and

said tablet is adapted for delivering said active ingredient to the bloodstream of a patient via the patient's buccal cavity.

16. A method of delivering an active ingredient to a person comprising administering the active ingredient via a progressive hydration bioadhesive tablet, wherein said tablet comprises an effective amount of the active ingredient selected from the group consisting of glycoproteins, proteins, sex hormones, anti-hormones, nitrates, beta-

agonists, beta-antagonists, opioids, opioid-antagonists, antidepressants, HMG CoA reductase inhibitors, antihistamines, ACE inhibitors, prostaglandins, and any other active ingredient which is metabolized or degraded by moisture, enzymes or pH, about 1% to about 50% by weight lactose, about .5% to about 10% by weight water insoluble cross-linked polycarboxylic polymer, and about 1% to about 75% by weight water soluble polymer.

17. The method of claim 16 wherein the active ingredient is testosterone.

18. A method of treating or preventing ischemia or Alzheimer's disease comprising administering to a patient a sustained release, progressive hydration bioadhesive tablet comprising a therapeutically effective amount of testosterone, about 1% to about 50% by weight lactose, about .5% to about 10% by weight water insoluble cross-linked polycarboxylic polymer, and about 1% to about 75% by weight water soluble polymer.

19. The method of claim 18 wherein the bioadhesive tablet is formulated for buccal administration.

20. The method of claim 18, wherein the bioadhesive tablet is formulated for vaginal administration.

21. A sustained release, progressive hydration bioadhesive tablet, comprising a therapeutically effective amount of an active ingredient selected from the group consisting of glycoproteins, proteins, sex hormones, anti-hormones, nitrates, beta-agonists, beta-antagonists, opioids, opioid-antagonists, antidepressants, HMG CoA reductase inhibitors, antihistamines, ACE inhibitors, prostaglandins, and any other active ingredient which is metabolized or degraded by moisture, enzymes or pH, about 1% to about 50% by weight lactose, about .5% to about 10% by weight water insoluble cross-linked polycarboxylic polymer, and about 1% to about 75% by weight water soluble polymer.

22. A method for preparing a sustained release, progressive hydration bioadhesive tablet, comprising combining an effective amount of an active ingredient selected from the group consisting of glycoproteins, proteins, sex hormones, anti-hormones, nitrates, beta-agonists, beta-antagonists, opioids, opioid-antagonists, antidepressants, HMG CoA reductase inhibitors, antihistamines, ACE inhibitors, prostaglandins, and any other active ingredient which is metabolized or degraded by moisture, enzymes or pH, together with about 1% to about 50% by weight lactose, about .5% to about 10% by weight water insoluble cross-linked polycarboxylic polymer and 1% to about 75% by weight water soluble polymer.

23. The tablet of claim 5, wherein the active ingredient is terbutaline.

24. The tablet of claim 23, wherein the cellulose is hydroxpropylmethyl cellulose, the starch is corn starch, the insoluble cross-linked polycarboxylic polymer is polycarbophil, the water soluble polymer is carbomer or Carbomer 974P, and the silica is silicon dioxide.

25. The tablet of claim 13, further comprising cellulose.

26. The tablet of claim 25, wherein the cellulose is hydroxpropylmethyl cellulose, the starch is corn starch, the insoluble cross-linked polycarboxylic polymer is polycarbophil, the water soluble polymer is carbomer or Carbomer 974P, and the silica is silicon dioxide.